Applicant:
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## Amendments to the claims

The following listing of claims replaces all earlier versions of the claims:

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- 1. (Original) A method of detecting similarity between protein sequences comprising comparing a first disulfide signature to a second disulfide signature, each disulfide signature being characteristic of a corresponding protein sequence.
- 2. (Original) The method of claim 1, wherein each disulfide signature describes a disulfide topology of the corresponding protein sequence.
- 3. (Original) The method of claim 1, wherein each disulfide signature includes the number of residues between a pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the next disulfide bridge in the corresponding protein sequence.
- 4. (Original) The method of claim 3, wherein each disulfide signature includes the number of residues between each pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the next disulfide bridge in the corresponding protein sequence, for each disulfide bridge in the corresponding protein sequence.
- 5. (Original) The method of claim 1, wherein comparing includes calculating a measure of similarity between the first disulfide signature and the second disulfide signature.
- 6. (Original) The method of claim 5, wherein comparing further includes calculating a measure of statistical relevance for the measure of similarity between the first disulfide signature and the second disulfide signature.
- 7. (Original) The method of claim 1, wherein comparing includes searching a database including a plurality of disulfide signatures, each disulfide signature of the database characteristic of a corresponding protein sequence.

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- 8. (Original) The method of claim 7, wherein comparing includes calculating a measure of similarity between the first disulfide signature and each of a plurality of disulfide signatures of the database.
- 9. (Original) The method of claim 7, wherein searching the database includes searching with a subpattern of the first disulfide signature.
- 10. (Original) The method of claim 9, wherein the subpattern is generated by calculating the disulfide signature that results when one or more disulfide bridges is removed from the protein sequence corresponding to the first disulfide signature.
- 11. (Original) The method of claim 7, wherein at least one disulfide signature in the database is associated with a sequence identifier.
- 12. (Original) The method of claim 7, wherein at least one disulfide signature in the database is associated with a domain identifier.
- 13. (Original) The method of claim 7, further comprising clustering disulfide signatures of the database.
- 14. (Original) The method of claim 13, wherein clustering includes grouping disulfide signatures by number of disulfide bridges.
- 15. (Original) The method of claim 13, wherein clustering includes grouping disulfide signatures by disulfide topology.
- 16. (Original) The method of claim 13, wherein clustering includes calculating a measure of similarity between disulfide signatures and grouping based on the measure of similarity.
- 17. (Original) A method of detecting similarity between protein sequences comprising: generating a database including a plurality of disulfide signatures, each disulfide signature being characteristic of a corresponding protein sequence; and

comparing a first disulfide signature corresponding to a protein sequence to at least one disulfide signature of the database.

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18. (Original) The method of claim 17, wherein each disulfide signature describes a disulfide topology of the corresponding protein sequence.

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- 19. (Original) The method of claim 18, wherein each disulfide signature includes the number of residues between a pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the next disulfide bridge in the corresponding protein sequence.
- 20. (Original) The method of claim 19, wherein each disulfide signature includes the number of residues between each pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the next disulfide bridge in the corresponding protein sequence, for each disulfide bridge in the corresponding protein sequence.
- 21. (Original) The method of claim 17, wherein generating the database includes identifying a disulfide bridge by protein sequence homology or protein structure homology.
- 22. (Original) The method of claim 17, wherein generating the database includes calculating a disulfide signature for a protein sequence.
- 23. (Original) The method of claim 17, wherein comparing includes calculating a measure of similarity between the first disulfide signature and the disulfide signature of the database.
- 24. (Original) The method of claim 23, wherein comparing further includes calculating a measure of statistical relevance for the measure of similarity between the first disulfide signature and the disulfide signature of the database.
- 25. (Original) The method of claim 17, wherein comparing includes comparing a subpattern of the first disulfide signature to at least one disulfide signature of the database.
- 26. (Original) The method of claim 25, wherein the subpattern is generated by calculating the disulfide signature that results when one or more disulfide bridges is removed from the corresponding protein sequence.

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27. (Original) The method of claim 17, wherein at least one disulfide signature of the database is associated with a sequence identifier.

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- 28. (Original) The method of claim 17, wherein at least one disulfide signature of the database is associated with a domain identifier.
- 29. (Original) The method of claim 18, further comprising clustering the disulfide signatures of the database.
- 30. (Original) The method of claim 29, wherein clustering includes grouping disulfide signatures by number of disulfide bridges.
- 31. (Original) The method of claim 29, wherein clustering includes grouping disulfide signatures by disulfide topology.
- 32. (Original) The method of claim 29, wherein clustering includes calculating a measure of similarity between at least one pair of disulfide signatures and grouping based on the measure of similarity.
- 33.-40. (Canceled)
- 41. (Original) A computer program for detecting similarity between protein sequences, the computer program comprising instructions for causing a computer system to compare a first disulfide signature to a second disulfide signature, each disulfide signature being characteristic of a corresponding protein sequence.
- 42. (Original) The computer program of claim 41, wherein each disulfide signature includes the number of residues between a pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the next disulfide bridge in the corresponding protein sequence.
- 43. (Original) The computer program of claim 42, wherein each disulfide signature includes the number of residues between each pair of cysteines joined by a disulfide bridge, and the number of residues between the first cysteine of each disulfide bridge and the first cysteine of the

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next disulfide bridge in the corresponding protein sequence, for each disulfide bridge in the corresponding protein sequence.

44. (Original) The computer program of claim 41, wherein comparing includes calculating a measure of similarity between the first disulfide signature and the second disulfide signature.

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- 45. (Original) The computer program of claim 44, wherein comparing further includes calculating a measure of statistical relevance for the measure of similarity between the first disulfide signature and the second disulfide signature.
- 46. (Original) The computer program of claim 41, wherein comparing includes searching a database including a plurality of disulfide signatures, each disulfide signature of the database characteristic of a corresponding protein sequence.
- 47. (Original) The computer program of claim 46, wherein searching the database includes searching with a subpattern of the first disulfide signature.
- 48. (Original) The computer program of claim 47, wherein the subpattern is generated by calculating the disulfide signature that results when one or more disulfide bridges is removed from the protein sequence corresponding to the first disulfide signature.
- 49. (Original) The computer program of claim 46, wherein at least one disulfide signature in the database is associated with a sequence identifier.
- 50. (Original) The computer program of claim 46, wherein at least one disulfide signature in the database is associated with a domain identifier.
- 51. (Original) The computer program of claim 46, further comprising clustering disulfide signatures of the database.
- 52. (Original) The computer program of claim 51, wherein clustering includes grouping disulfide signatures by number of disulfide bridges.
- 53. (Original) The computer program of claim 51, wherein clustering includes grouping disulfide signatures by disulfide topology.

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(Original) The computer program of claim 51, wherein clustering includes calculating a 54. measure of similarity between disulfide signatures and grouping based on the measure of similarity.

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55.-67. (Canceled)

- 68. (Original) A method of describing a protein sequence comprising generating a first disulfide signature, the disulfide signature describing the cysteine spacing and disulfide topology of first a protein sequence.
- 69. (Original) The method of claim 68, further comprising identifying a disulfide bridge by protein sequence homology or protein structure homology.
- (Original) The method of claim 68, further comprising generating a second disulfide 70. signature, the signature describing the cysteine spacing and disulfide topology of a second protein sequence.
- (Original) The method of claim 70, further comprising comparing the first disulfide 71. signature to a second disulfide signature.
- (Original) The method of claim 71, wherein comparing includes calculating a measure of 72. similarity between the first disulfide signature and the second disulfide signature.
- (Original) The method of claim 71, further comprising generating a database including 73. the first and second disulfide signatures.